PATENT COOPERATION TREATY

From the INTERNATIONAL SE HING AUTHORITY

China Patent Agent (H.K.) Ltd. 22/F, Great Eagle Centre 23 Harbour Road, Wanchai



## NOTIFICATION OF TRANSMITTAL OF THE INTERNATIONAL SEARCH REPORT OR THE DECLARATION

Hong Kong Special Administrative Region, P.R.China	(PCT Rule 44.1)				
	Date of mailing (day/month/year) 2 4 DFC 1938 (24.12.98)				
Applicant's or agent's file reference FPCH981629P	FOR FURTHER ACTION See paragraphs 1 and 4 below				
International application No. PCT/CN98/00052	International Filing date (day/month/year) 31 MAR 1998 (31.03.98)				
Applicant • TONGHUA GANTECH I	BIOTECHNOLOGY LTD. et al				

		TONGHUA GANTECH BIOTECHNOLOGY LTD. et al
1.	$\boxtimes$	The applicant is hereby notified that the international search report has been established and is transmitted herewith.
		Filing of amendments and statement under Article 19:
		The applicant is entitled, if he so wishes, to amend the claims of the international application (see Rule 46):  When? The time limit for filing such amendments is normally 2 months from the date of transmittal of the international search report; however, for more details, see the notes on the accompanying sheet.  Where? Directly to the International Bureau of WIPO
		34, Chemin des Colombettes
		1211 Geneva 20, Switzerland
		Facsimile No.: (41-22)740.14.35
		For more detailed instructions, see the notes on the accompanying sheet.
2.		The applicant is hereby notified that no international search report will be established and that the declaration under Article 17(2)(a) to that effect is transmitted herewith.
3.		With regard to the protest against payment of (an) additional fee(s) under Rule 40.2, the applicant/is notified that:
		the protest together with the decision thereon has been transmitted to the International Bureau together with the applicant's request to forward the texts of both the protest and the decision thereon to the designated Offices.
4.	Fur	no decision has been made yet on the protest; the applicant will be notified as soon as a decision is made.  ther action(s): The applicant is reminded of the following:
	Shor	tly after 18 months from the priority date, the international application will be published by the International Bureau. If the applicant wishes to avoid or postpone publication, a notice of withdrawal of the international application, or of the priority claim, must reach the International Bureau as provided in Rules 90bis.1 and 90bis.3, respectively, before the completion of the technical preparations for international publication.
	Witl	nin 19 months from the priority date, a demand for international preliminary examination must be filed if the applicant wishes to postpone the entry into the national phase until 30 months from the priority date(in some Office even later).
	With	hin 20 months from the priority date, the applicant must perform the prescribed acts for entry into the national phase before all designated Offices which have not been elected in the demand or in a later election within 19 months from the priority date or could not be elected because they are not bound by Chapter II.

Name and mailing address of the ISA/

The Chinese Patent Office 6, Xitucheng Road, Haidian District Beijing 100088, P.R.China No. 86-10-62019451

Facsimile No.

Authorized officer

ZHOU LI

Telephone No. 86-10-62093058



## NOTES TO FORM PCT/ISA 220

These Notes are intended to go be basic instructions concerning the filing of an enents under Article 19. The Notes are based on the requirements of the Patent Cooperation Treaty, the Regulations and the Administrative Instructions under that Treaty. In case of discrepancy between these Notes and those requirements, the latter are applicable. For more detailed information, see also the PCT Applicant's Guide, a publication of WIPO.

In these Notes, "Article," "Rule" and "Section" refer to the provisions of the PCT, the PCT Regulations and the PCT Administrative Instructions, respectively.

#### INSTRUCTIONS CONCERNING AMENDMENTS UNDER ARTICLE 19

The applicant has, after having received the international search report, one opportunity to amend the claims of the international application. It should however be emphasized that, since all parts of the international application (claims, description and drawings) may be amended during the international preliminary examination procedure, there is usually no need to file amendments of the claims under Article 19 except where, e.g. the applicant wants the latter to be published for the purposes of provisional protection or has another reason for amending the claims before international publication. Furthermore, it should be emphasized that provisional protection is available in some states only.

#### What parts of the international application may be amended?

Under Article 19, only the claims may be amended.

During the international phase, the claims may also be amended (or further amended) under Article 34 before the International Preliminary Examining Authority. The description and drawings may only be amended under Article 34 before the International Preliminary Examining Authority.

Upon entry into the national phase, all parts of the international application may be amended under Article 28 or, where applicable, Article 41.

When? Within 2months from the date of transmittal of the international search report or 16 months from the priority date, whichever time limit expires later. It should be noted, however, that the amendments will be considered as having been received on time if they are received by the International Bureau after the expiration of the applicable time limit but before the completion of the technical preparations for international publication (Rule 46.1).

#### Where not to file the amendments?

The amendments may only be filed with the International Bureau and not with the receiving Office of or the International Searching Authority (Rule 46.2).

Where a demand for international preliminary examination has been/is filed, see below.

How? Either by cancelling one or more entire claims, by adding one or more new claims or by amending the text of one or more of the claims as filed.

A replacement sheet must be submitted for each sheet of the claims which, on account of an amendment or amendments, differs from the sheet originally filed.

All the claims appearing on a replacement sheet must be numbered in Arabic numerals. Where a claim is cancelled, no renumbering of the other claims is required. In all cases where claims are renumbered, they must be renumbered consecutively (Administrative Instructions, Section 205(b)).

The amendments must be made in the language in which the international application is to be published.

### What documents must/may accompany the amendments?

#### Letter (Section 205(B)):

The amendments must be submitted with a letter.

The letter will not be published with the international application and the amended claims. It should not be confused with the "Statement under Article 19(1)" (see below, under "Statement under Article 19(1)").

The letter must be in English or French, at the choice of the applicant. However, if the language of the international application is English, the letter must be in English; if the language of the international application is French, the letter must be in French.

Notes to Form PCT/ISA/220 (first sheet) (July 1998)

#### NOTES TO FORM PCT/ISA 220(continued)

The letter must indicate the differences between the claims as filed and the claims as amended. It must, in particular, indicate, in connection with each claim appearing in the international application (it being understood that identical indications concerning several claims may be grouped), whether

- (i) the claim is unchanged;
- (ii) the claim is cancelled;
- (iii) the claim is new;
- (iv) the claim replaces one or more claims as filed;
- (v) the claim is the result of the division of a claim as filed.

## The following examples illustrate the manner in which amendments must be explained in the accompanying letter:

- 1. [where originally there were 48 claims and after amendment of some claims there are 51]:
  - "Claims 1 to 29,31,32,34,35,37 to 48 replaced by amended claims bearing the same numbers; claims 30,33 and 36 unchanged; new claims 49 to 51 added."
- 2. [where originally there were 15 claims and after amendment of all claims there are 11]:
  - "Claims 1 to 15 replaced by amended claims 1 to 11."
- 3. [Where various kinds of amendments are made]:
  - "Claims 1-10 unchanged; claims 11 to 13,18 and 19 cancelled; claims 14,15 and 16 replaced by amended claim 14; claim 17 subdivided into amended claims 15,16 and 17; new claims 20 and 21 added."

#### "Statement under Article 19(1)"(Rule 46.4)

The amendments may be accompanied by a statement explaining the amendments and indicating any impact that such amendments might have on the description and the drawings (which cannot be amended under Article 19(1)).

The statement will be published with the international application and the amended claims.

### It must be in the language in which the international application is to be published.

It must be brief, not exceeding 500 words if in English or if translated into English.

It should not be confused with and does not replace the letter indicating the differences between the claims as filed and as amended. It must be filed on a separate sheet and must be identified as such by a heading, preferably by using the words "Statement under Article 19(1)."

It may not contain any disparaging comments on the international search report or the relevance of citations contained in that report. Reference to citations, relevant to a given claim, contained in the international search report may by made only in connection with an amendment of that claim.

#### Consequence if a demand for international preliminary examination has already been filed

If, at the time of filing any amendments and any accompanying statement, under Article 19, a demand for international preliminary examination has already been submitted, the applicant must preferably, at the time of filing the amendments (and any statement) with the International Bureau, also file with the International Preliminary Examining Authority a copy of such amendments (and of any statement) and, where required, a translation of such amendments for the procedure before that Authority (see Rules 55.3(a) and 62.2, first sentence). For further information, see the Notes to the demand form (PCT/IPEA/401).

## Consequence with regard to translation of the international application for entry into the national phase

The applicant's attention is drawn to the fact that, upon entry into the national phase, a translation of the claims as amended under Article 19 may have to be furnished to the designated/elected Offices, instead of ,or in addition to, the translation of the claims as filed.

For further details on the requirements of each designated/elected Office, see the PCT Applicant's Guide, Volume II.

Notes to Form PCT/ISA/220 (second sheet) (July 1998)



## INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

Applicant's or agent's file reference		
FPCH981629P		Transmittal of International SearchReport 20) as well as, where applicable, item 5below.
International application No.	International filing date(day/month/year)	(Earliest)Priority Date(day/month/year)
PCT/CN98/00052	31 MAR 1998 (31.03.98)	
Applicant		
TONGHU	A GANTECH BIOTECHNOLOG	GY LTD. et al
according to Article 18. A copy is being This international search report consists		ets.
It is also accompanied by a co	py of each art document cited in this rep	port.
1. Certain claims were found u	nsearchable(See Box I)	,
2. Unity of invention is lacking	(See Box II)	
3. The international application of international search was carried	contains disclosure of a nucleotide and out on the basis of the sequence listin	or amino acid sequence listing and the
	d with the international application.	
furn	nished by the applicant separately from	• •
trar	]but not accompanied by a state going beyond the disclosure in ascribed by this Authority.	ment to the effect that it did not include matter at the international application as filed.
4. With regard to the title, the	text is approved as submitted by the appli	cant.
the	text has been established by this Authority	to read as follows:
5. With regard to the abstract,	text is approved as submitted by the appli	cant.
the Box	text has been established, according to Ru	le 38.2(b), by this Authority as it appears in from the date of mailing of this international
6. The figure of the drawings to be publ	ished with the abstract is:	
Figure No. as	suggested by the applicant.	None of the figures.
bec	cause the applicant failed to suggest a fi	gure.
bec	cause this figure better characterizes the	invention.

# INTERNAT VAL SEARCH REPORT Information patent family members

pational application No. PCT/CN98/00052

Patent document cited in search report	Publication date	Patent family members	Publication date		
WO-A-9620724	11-07-1996	ZA-A- 9500142 AU-A- 1550095	25-09-1996 24-07-1996		
		PL-A- 321039	24-11-1997		
WO-A-9718233	22-05-1997	AU-A- 7659696	05-06-1997		

## INTERNAT NAL SEARCH REPORT

PCT/CN98/00052

## A. CLASSIFICATION OF SOJECT MATTER

IPC6 C07K19/00,14/62,14/61,C12N15/62,C12N1/21(C12N1/21,C12R1:19)

According to International Patent Classification(IPC) or to both national classification and IPC

#### **B.** FIELDS SEARCHED

Minimum documentation searched(classification system followed by classification symbols)

IPC<sup>6</sup> C07K,C12N

Documentation searched other than minimum documentation to the extent that such documents are included in the field searched

#### CNPAT, Chinese Scientific and Technical Journals

Electronic data base consulted during the international search(name of data base and, where practicable, search terms used)
GenBank CDS translations, PDB, SwissProt, SPupdate, PIR, WPI, DIALOG (files 5,155,357,358)
(chimeric, chaperone, insulin, proinsulin, insulin precursor, growth hormone, somatotropin, fold, folding)

C. DOCUMENTS CONSIDERED TO BE RELEVANT  Category*  Citation of document, with indication, where appropriate, of the relevant passages  Relevant class and the relevant passages  Relevant class and the relevant passages  Relevant class and the relevant passages  A WO,A,96 20724 (BIO-TECHNOLOGY GENERAL CORP.)  1-29,38  11 July 1996  see the whole document  Y Figure 1,2,6,7, page 4 line 35-page 5 line 17, page 13 lines 14-26, 30-37,4; Example 3  Y WO,A,97 18233 (PHARMACIA & UPJOHN AB) 22 May 1997  see the whole document, especially page 4 line 14-page 6 line 8  Further document defining the general state of the art which is not considered to be of particular relevance:  "A" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason(as specified)  "Co document referring to an oral disclosure, use, exhibition or other means "be ocument referring to an oral disclosure, use, exhibition or other means "be ocument published prior to the international filing date but later than the priority date claimed  Date of the actual completion of the international search 16 December 1998 (16. 12. 98)  Relevant class and the relevant constitution of the relevant class and the relevant passages Relevant class 44,46,47,50  1-29,38  44,46,47,50  48,49,52-6  See patent family annex.  **  **  **  **  **  **  **  **  **	
A WO,A,96 20724 (BIO-TECHNOLOGY GENERAL CORP.)  1-29,38 11 July 1996  see the whole document  Y Figure1,2,6,7, page 4 line 35-page 5 line 17, page 13 lines 14-26, Example 3  Y WO,A,97 18233 (PHARMACIA & UPJOHN AB) 22 May 1997  see the whole document, especially page 4 line 14-page 6 line 8  WO,A,97 18233 (PHARMACIA & UPJOHN AB) 22 May 1997  see the whole document, especially page 4 line 14-page 6 line 8  Secial categories of cited documents:  "A" document defining the general state of the art which is not considered to be of particular relevance:  "E" earlier document but published on or after the international filing date document of particular relevance; the claimed invention special reason(as specified)  "O document referring to an oral disclosure, use, exhibition or other means "P" document referring to a no ral disclosure, use, exhibition or other means "P" document published prior to the international filing date but later than the priority date claimed  Date of the actual completion of the international search  Date of the actual completion of the international search  1-29,38  44,46,47,50  71-7  30-37,4:  48,49,52-6  """  See patent family annex.  """  "ater document published after the international filing date date and not in conflict with the application but cited to document of particular relevance; the claimed invention considered to involve an inventive step when the document of particular relevance; the claimed invention considered to involve an inventive step when the document the priority date claimed  Date of the actual completion of the international search	
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See the whole document  Y Figure 1, 2, 6, 7, page 4 line 35-page 5 line 17, page 13 lines 14-26, Example 3  Y WO,A, 97 18233 (PHARMACIA & UPJOHN AB) 22 May 1997 See the whole document, especially page 4 line 14-page 6 line 8  Further documents are listed in the continuation of Box C.  See patent family annex.  * Special categories of cited documents: "A" document defining the general state of the art which is not considered to be of particular relevance. "E" carlier document but published on or after the international filing date to be of particular relevance to the principle or theory underlying the invention considered novel or cannot be considered to involve an special reason(as specified) "O" document of particular relevance; the claimed invention considered novel or cannot be considered to involve an step when the document is taken alone in document of particular relevance; the claimed invention considered to involve an an eventive step when the document of particular relevance; the claimed invention considered to involve an inventive step when the document of particular relevance; the claimed invention considered to involve an inventive step when the document of particular relevance; the claimed invention considered to involve an inventive step when the document of particular relevance; the claimed invention considered to involve an inventive step when the document of particular relevance; the claimed invention considered to involve an inventive step when the document of particular relevance; the claimed invention considered to involve an inventive step when the document of particular relevance; the claimed invention considered to involve an inventive step when the document of particular relevance; the claimed invention considered to involve an inventive step when the document of particular relevance; the claimed invention considered to involve an inventive step when the document of particular relevance; the claimed invention considered to involve an anneal state alone.  "T" later document published after	-42,
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Y WO,A,97 18233 (PHARMACIA & UPJOHN AB) 22 May 1997  see the whole document, especially page 4 line 14-page 6 line 8  Further documents are listed in the continuation of Box C.  See patent family annex.  The later document published after the international filing date date and not in conflict with the application but cited to the principle or theory underlying the invention document defining the general state of the art which is not considered to be of particular relevance:  "E" earlier document but published on or after the international filing date date and not in conflict with the application but cited to the principle or theory underlying the invention document of particular relevance; the claimed invention considered novel or cannot be considered to involve an step when the document is taken alone document referring to an oral disclosure, use, exhibition or other means "P" document published prior to the international filing date but later than the priority date claimed  Date of the actual completion of the international search  Date of mailing of the international search report	<u>3,45,</u>
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"P" document published prior to the international filing date but later than the priority date claimed  "&" document member of the same patent family  Date of the actual completion of the international search  Date of mailing of the international search	
16 December 1998 (16, 12, 98) 2 4 DFC 1999 (2 4 1 2 00)	
(2 4, 7 4, 70)	
Name and mailing address of the ISA/  The Chinese Patent Office 6, Xitucheng Road, Haidian District, Beijing, 100088, China  Facsimile No. 86-10-62019451  Authorized officer  ZHOU LI  Telephone No. 86-10-62093058	\$2.535 <b>68</b> 555



a special address to which correspondence should be sent.

## REQUEST

International Application N					
International Filing Date					
•					
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Name of receiving Office and "PCT International Application"					

The undersigned requests that the present international application be rocessed according to the Patent Cooperation Treaty. Applicant's or agent's file reference FPCH981629P (if desired)(12 characters maximun) Box No.I TITLE OF INVENTION CHIMERIC PROTEIN CONTAINING AN INTRAMOLECULAR CHAPERONE-LIKE SEQUENCE AND ITS APPLICATION TO INSULIN PRODUCTION Box No.II APPLICANT Name and address: (Family name followed by given name; for a legal entity, full offical designation. The address must include postal code and name of country. The country of the address indicated in this Box is the applicant's Sate(i.e. country) of residence if no State of residence is indicated below) This person is also inventor. TONGHUA GANTECH BIOTECHNOLOGY LTD. Telephone No. 0435-5858801 Gantech Biotechnology, Dongbao Group, Tonghua City Facsimile No. 0435-5858585 Jilin Province,134102 China Teleprinter No. State (i.e. country) of residence:CN State (i.e. country) of nationality:CN the States indicated in the United States all designated States except This person is applicant for the Supplemental Box all designated of America only the United States of America States the purpose of: FURTHER APPLICANT(S) AND/OR (FURTHER) INVENTOR(S) Box No. III Name and address: (Family name followed by given name; for a legal entity, full offical designation. The address must include postal code and name of country. The country of the address indicated in this Box is the applicant's State(i.e. country) of residence if no State of residence is indicated below) This person is: applicant only applicant and inventor GAN, Zhongru Gantech Biotechnology, Dongbao Group, Tonghua City inventor only(if this check-box is Jilin Province, 134102 China marked, do not fill in below) State (i.e. country) of residence:CN State (i.e. country) of nationality: CN the States indicated in the United States all designated States except This person is applicant for all designated the Supplemental Box of America only the United States of America States the purpose of: Further applicants and/or (furhter) inventors are indicated on a continuation sheet AGENT OR COMMON REPRESENTATIVE: OR ADDRESS FOR CORRESPONDENCE Box No. IV The person identified below is hereby/has been appointed to act on behalf common representative 🔀 agent of the applicants(s) before the competent International Authorities as: Name and address: (Familly name followed by given name; for a legal entity, full offical Telephone No. (852)28284688 designation. The address must include postal code and name of country) China Patent Agent (H.K.) Ltd. Facsimile No. (852)28271018 22/F, Great Eagle Centre 23 Harbour Road, Wanchai Hong Kong Special Administrative Region, Teleprinter No. The People's Republic of China Mark this check-box where no agent or common representative is/has been appointed and the space above is used instead to indicate

Boa No. V	DESIGNATION OF STATES							
The following	ing designations are hereby under Rule 4.9(a) (n	nark the a	applicable check-box least one must be marked):					
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⊠EP	European Patent: AT Austria, BE Belgiun, CH and LI Switzerland and Liechtenstein, DE Germany, DK Denmark, ES Spain, FI Finland, FR France, GB United Kingdom, GR Greece, IE Ireland, IT Italy, LU Luxembourg, MC Monaco, NL Netherlands, PT Portugal, SE Sweden, and any other State which is a Contracting State of the Eruropean Patent Convention and of the PCT,							
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The applicant declares that those additional designations are subject to confirmation and that any designation which is not confirmed before the expirations of 15 months from the priority date is to be regarded as withdrawn by the applicant at the expiration of that time limit. (Confirmation of a designation consists of the filing of a notice specifying that designation and the payment of the designation and confirmation fees. Confirmation must reach the receiving Office within the 15-month time limit)

2. Description: 31 sheets 3. claims: 9 sheets 3. □ Copy of general power of attorney 3. □ Copy of general power of deposited microorganisms 3. □ Statement explaining lack of deposited and/or amino acid	x No. VI PRIORITY	CLAIN			Further prior	ity claims	Cated		lemental Box
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Applicant's or agent's file reference FPCH981629P	Date stamp of the receiving Office					
Applicant TONGHUA GANTECH BIOTECHNOLOGY LTD.						
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1. TRANSMITTAL FEE	CNY 500 T					
2. SEARCH FEE	CNY 800 S					
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(Applicants from certain States are entitled to a reduction of 75% of the international fee. Where the applicant is (or all applicants are) so entitled, the total to be entered at I is 25% of the sum of the amounts entered at B and D.)						
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is hereby authorized to charge the fee for prep Bureau of WIPO to my deposit account.	paration and transmittal of the priority document to the International					
March 30, 1998						

Date(day/month/year)

Signature

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- (51)<sup>6</sup> C07K 16/00, 16/18, 16/44, C12Q 1/68, G01N 33/567
- (11) WO 99/50300

(13) A1

- (21) PCT/US99/06710
- (22) 29 Mar/mar 1999 (29.03.1999)

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- (43) 7 Oct/oct 1999 (07.10.1999)
- (54) METHOD OF IDENTIFYING, DIAGNOSING AND TREATING SYNU-CLEIN POSITIVE NEURODEGENE-RATIVE DISORDERS
  - METHODE D'IDENTIFICATION, DE DIAGNOSTIC ET DE TRAITEMENT DE TROUBLES NEURODEGENE-RATIFS A NIVEAUX ELEVES DE SYNUCLEINE
- (63) US 60/080,015 (CIP) 30 Mar/mar 1998 (30.03.1998) US 60/095,383 (CIP) 5 Aug/août 1998 (05.08.1998)
- (71) THE TRUSTEES OF THE UNIVER-SITY OF PENNSYLVANIA [US/US]; Center for Technology Transfer, Suite 300, 3700 Market Street, Philadelphia, PA 19104 (US).

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- (81) AU CA JP US; EP (AT BE CH CY DE DK ES FI FR GB GR LE IT LU MC NL PT SE).

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- (54) EPITOPES IN VIRAL ENVELOPE PROTEINS AND SPECIFIC ANTIBO-DIES DIRECTED AGAINST THESE EPITOPES: USE FOR DETECTION OF HCV VIRAL ANTIGEN IN HOST TISSUE
  - EPITOPES DE PROTEINES EN-VELOPPES VIRALES, ANTICORPS SPECIFIQUES DE CES PROTEINES ET LEUR UTILISATION DANS LA DETECTION D'ANTIGENES DU VHC DANS DES TISSUS HOTES
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- (51)<sup>6</sup> C07K 19/00, 14/62, 14/61, C12N 15/62, 1/21 // (C12N 1/21, C12R 1:19)
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- (54) CHIMERIC PROTEIN CONTAI-NING AN INTRAMOLECULAR CHAPERONE-LIKE SEQUENCE AND ITS APPLICATION TO INSULIN PRO-DUCTION
  - PROTEINE CHIMERE CONTENANT UNE SEQUENCE DE TYPE CHA-PERON INTRAMOLECULAIRE ET SON APPLICATION DANS LA PRO-DUCTION D'INSULINE
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- (54) IMMUNE RESPONSE MODULATOR ALPHA-2 MACROGLOBULIN COMPLEX
  - COMPLEXE \ D'ALPHA-2 MACRO-GLOBULINE MODULATEUR DE LA REPONSE IMMUNITAIRE
- (63) US

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